multiorgan failure) are alive with a median follow up of 2 years (range, 10 days–5 years) and a 3-yr OS by Kaplan Meier analysis of 96% (95%CI: 73%-99%). All patients with viral infections at the time of transplant cleared the infection at a median time of 51 days (range, 44-54). ELISPOT analyses of peripheral blood at the time that infections responded showed significant T cell responses against the pertinent viruses. All evaluable patients have normalization of their immune or metabolic defect including adequate B cell function in SCID patients. Hence, UCBT after full intensity conditioning without serotherapy for pediatric non-malignant diseases can produce rapid functional engraftment and immune-reconstitution in the absence of significant GVHD, leading to excellent overall survival.

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Chemotherapy-Only Preparative Regimen for Alternative Donor Hematopoietic Cell Transplantation for Patients with Fanconi Anemia (FA): Results of a Multi-Institutional Study

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Objective: This multi-institutional study was designed to optimize outcomes of alternative donor HCT in patients with FA without using total body irradiation (TBI). TBI was replaced by busulfan (BU) (to reduce the risk of secondary solid tumors) and BU dose was reduced after first 25 patients to find the lowest acceptable BU dose.

Methods: 45 patients were transplanted from June 2009 to May 2014. These included patients with prior transfusions, androgen use and myelosdysplastic syndrome. Patient demographics, disease and donor characteristics are described in Table 1.

Table 1
Patient demographics

Characteristics	Number/Median (Range)
Median age in years	8.2 (4.3-44)
<10 years of age	27
≥10 years of age	18
Gender	
- Males	20
- Females	25
Severe Single Lineage Cytopenia	5
Severe Aplastic Anemia	29
Myelodysplastic Syndrome	11
- Low grade	7
- High grade	4
Donor type	
Matched Unrelated (8/8 match)	25
Mismatched Unrelated (7/8 match)	14
Mismatched Related (4/8, 5/8, 6/8 match)	5
Phenotypically Matched Related (8/8)	1
Follow-up in months, Median and Range	21.3 (2.6 - 61)

Table 2
Patient outcomes

Characteristic	Number/Median (range)
Days to Neutrophil engraftment	9 (7-15)
Days to Platelet engraftment	16 (11-230)
Complication	
Oral mucositis	23
Hyperbilirubinemia	10
Hypertension	12
Sinusoidal obstruction syndrome (SOS)*	1
Infections (number of patients)	26
- Bacterial	11
- Viral	21
- Fungal	3
GVHD	
Acute GVHD	
- Acute Gr I-II	4
- Acute Gr III-IV	0
Chronic GVHD	
- Chronic, limited	3
- Chronic, extensive	0

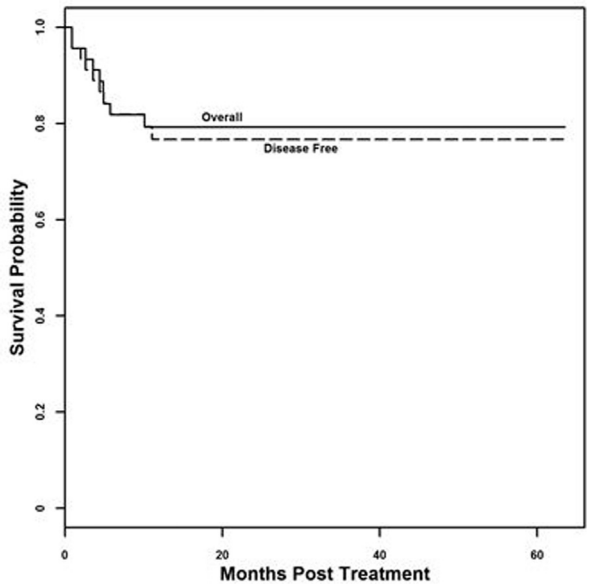

Fig 1. One-year probabilities of overall survival and disease free survival.

Preparative regimen included: BU (BU) 0.8-1.0 mg/Kg/dose IV (first 25 patients) and 0.6-0.8 mg/kg/dose Q 12H (next 20 patients) x 4 doses, cyclophosphamide (10mg/kg/dose), fludarabine (35mg/m2/dose) and rabbit ATG(2.5mg/kg/dose) daily x 4 days. BU doses were adjusted based on pharmacokinetics of the first dose. All grafts were T-cell depleted using the CliniMacs CD34 columns (Miltenyi). GvHD prophylaxis was cyclosporine.

Results: 43 patients engrafted. One patient had late graft failure and one had early relapse of MDS. See Table 2 for detailed results and transplant outcomes. One patient (#3) developed sinusoidal obstruction syndrome of liver. However, after reducing the BU goal level, no further SOS observed.

36 of the 45 patients are alive. Causes of death included infection (n=5), multi-organ failure (n=3), and severe pulmonary hypertension (n=1). One year probability of overall and disease free survival for the entire cohort was 79.2% (+/-6.2%) and 76.7 (+/-6.5%) respectively (Fig 1). OS for patients <10 years of age transplanted for marrow failure was 91.3% (+/-5.9%) similar to that reported for historical matched sibling donor HCT outcomes.

Conclusion: This chemotherapy only preparative regimen leads to excellent outcomes in patients undergoing

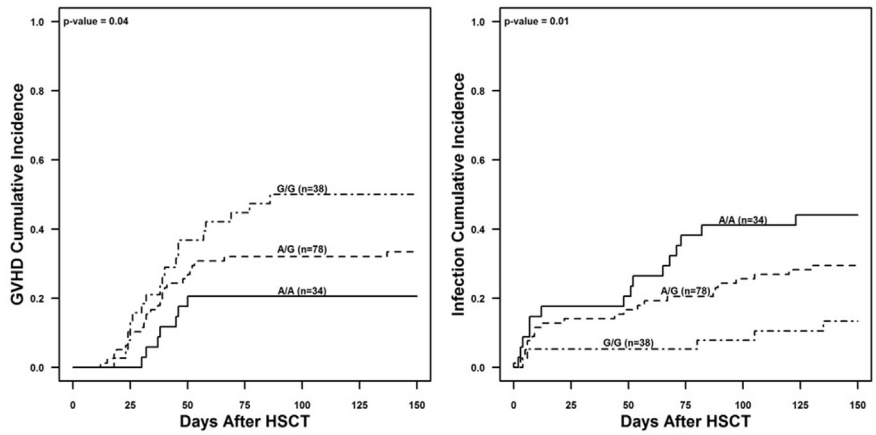

Figure.

alternative donor HCT for FA, comparable to historical TBI-based protocols, while avoiding short and (to date) long-term toxicity associated with radiation.

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Genetic Modifier of the Gut Microbiome, GvHD and Bacterial Translocation Following HSCT

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The human gut microbiome is involved in vital biological functions such as maintenance of immune homeostasis, modulation of intestinal development and enhanced metabolic capabilities. Disturbances of intestinal microbiota have been associated with development and progression of inflammatory conditions including GVHD. Non-secretor individuals do not express the H antigen on mucosal surfaces and body fluids due to a homozygous single nucleotide polymorphism in the fucosyltransferase 2 (FUT2) gene (428G>A) and FUT2 genotype has been shown to modify the gut microbiome. We hypothesized that FUT2 genotype influences risk of GVHD and bacterial translocation following allogeneic HSCT.

FUT2 genotype was determined in 150 consecutive patients receiving allogeneic HSCT at our center. We abstracted clinical characteristics and outcomes from the transplant database.

Median age at transplantation was 6.31 years and male/female ratio was 97/53. Genetic analysis revealed 23% recipients had A/A genotype (n=34), 52% A/G genotype (n=78) and 25% G/G genotype (n=38); Hardy Weinberg equilibrium was confirmed. Hematologic malignancies comprised 30% (n=45), 29% immune deficiencies (n=43), 22% bone marrow failure (n=33), 12% hemophagocytic lymphohistiocytosis (HLH) (n=18), 4% metabolic diseases (n=6), 3% hemoglobinopathies (n=4), and one patient with Evan's syndrome. 54% received myeloablative conditioning (n=81), while 46% received reduced intensity conditioning (n=68). Stem cell source was bone marrow in 81% (n=122), peripheral blood stem cells in 11% (n=16), cord blood in 7% (n=11), and one patient received both bone marrow and cord blood from a sibling donor. Among donors, 29% were matched sibling donors (n=43), 49% matched unrelated or other family member donors (n=74) and 22% were mismatched donors (n=33). Acute GVHD occurred in 36% of patients (n=54). Cumulative risk of any acute GVHD varied by FUT2 genotype with decreased risk in those with A/A genotype and increased risk in those with G/G genotype (p=0.04) (Fig. 1). A/A genotype (OR=0.4 p-value=0.046), myeloablation (OR=1.99 p-value=0.029) and matched sibling donor (OR=0.41 p-value=0.026) were identified to be significant GVHD risk factors in multivariate analysis. Bacteremia occurred in 34% of patients (n=51), and in contrast to our findings in GVHD cumulative incidence was increased in A/A genotype (p-value=0.01) (Fig. 1). A/A genotype (OR=3.94 p-value=0.0047) and A/G genotype (OR=2.46 p-value=0.05) were associated with increased risk in multivariate analysis.

FUT2 genotype influences risk of acute GVHD and bacteremia following HSCT. We hypothesize that the mechanism involves altered composition and diversity of gut microbiome, and limited data indicate increased diversity of the gut microbiome in the A/A genotype, but this requires additional studies.

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Risk Factors Predicting Outcomes of Autologous Hematopoietic Cell Transplantation (autoHCT) in Children, Adolescents and Young Adults (CAYA) with Relapsed/Refractory (Rel/Ref) Classical Hodgkin Lymphoma (HL): A CIBMTR Analysis

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Introduction: AutoHCT is a potentially curative modality for Rel/Ref HL. However, large studies evaluating the risk factors predicting outcomes of autoHCT in CAYA with Rel/Ref HL have not been performed.